

REMARKS

Applicants request consideration on the merits of the above-referenced patent application.

I. Amendments to the Claims

Claims 7, 12-14, 33, 38-40, 56 and 58 have been canceled without prejudice to their patentability. Claims 1, 13, 14, 20, 24, 28, 29, 39, 40, 46, 50, 54, 55 and 57 have been amended. Upon entry of this amendment, claims 1-6, 8-11, 15-32, 34-37, 41-55 and 57 will be pending. Applicants submit that amendments do not introduce new matter. Specifically:

Claims 1, 13, 20, 29, 46, 55 and 57 have been amended to characterize the selective cyclooxygenase-2 inhibitory drug D₉₀ particle size range as about 450 nm to about 900 nm. This amendment is supported by Applicants' specification at, for example, page 14, lines 3-6, page 50, lines 19-24, and claim 1 as originally filed.

Claims 14, 39 and 40 have been amended to characterize the upper limit of the selective cyclooxygenase-2 inhibitory drug weight average particle size as about 900 nm. This amendment is supported by Applicant's specification at, for example, page 14, lines 3-6, and claim 14 as originally filed.

Claims 24, 28, 50 and 54 have been amended to replace "in the" with "from" to correct an obvious grammatical error. The amended claims are supported by Applicants' specification at, for example, page 24, lines 9-12.

Other amendments simply rephrase the claims, remove redundancies or unnecessary terms, or correct grammatical or obvious errors. Applicants submit that such amendments do not affect the scope of the claims, and are permissible under MPEP § 2163.07.

Applicants reserve the right to pursue any canceled subject matter and/or any other subject matter disclosed in this application in one or more later-filed divisional and/or continuation applications.

II. Rejection of claims 1-58 under 35 U.S.C. § 103(a)

Claims 1-58 stand rejected under 35 U.S.C. § 103(a) as obvious over Black (EPO Document No. 0 863 134 A1) in view of Guess *et al.* (U.S. Patent No. 6,054,455) and Bagchi *et al.* (U.S. Patent No. 5,662,883). Reconsideration and withdrawal of the rejection is respectfully

requested. Applicants have canceled claims 7, 12-14, 33, 38-40, 56 and 58, thereby mooting the rejection as to those claims. As to claims 1-6, 8-11, 15-32, 34-37 and 41-55 and 57, Applicants submit that the subject matter is patentable over the cited references for at least the following reasons:

In order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the teachings of prior art references. When combined, the references must teach all of the claim limitations. *See* MPEP § 2143.

A. Claim 1

Amended claim 1 is directed to a composition comprising a selective cyclooxygenase-2 inhibitory low water soluble drug having a D_{90} particle size of from about 450 nm to about 900 nm and a second drug selected from a vasomodulator or an alkylxanthine compound. The composition is further characterized in that it exhibits a rapid therapeutic effect such that the formulations of the present invention provide a greater C_{max} and/or substantially shorter T_{max} by comparison to an otherwise similar composition having a particle size larger than 1000 nm. Applicants have also found that this formulation provides substantially similar C_{max} and/or at most a substantially similar T_{max} by comparison with an otherwise similar composition having a particle size smaller than 400 nm.

The principle reference, Black (EPO Document No. 0 863 134 A1) discusses the synthesis and use of a cyclooxygenase inhibitor, 2-(3,5-difluorophenyl)-3-(4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one. However, the reference fails to provide any teaching, suggestion or motivation of a selective cyclooxygenase-2 inhibitory low water soluble drug with D_{90} particle size of about 450 nm to about 900 nm. Nor does Black teach, suggest, or provide motivation for the rapid bioavailability, *i.e.* a greater C_{max} and/or substantially shorter T_{max} , of a drug of this formulation. Accordingly, Applicants respectfully submit that claim 1 is patentable over Black.

Guess *et al.* discuss a method for treating or preventing chronic non-bacterial prostatitis and prostatodynia with a tachykinin receptor agonist. Guess *et al.* further discuss the combination of the tachykinin receptor agonist with a plethora of compounds, including selective cyclooxygenase-2 inhibitors, for treating or preventing chronic non-bacterial prostatitis and

prostatodynia. Guess *et al.*, however, fail to teach, suggest, or provide motivation for a composition of selective cyclooxygenase-2 inhibitory low water soluble drug with D₉₀ particle size of about 450 nm to about 900 nm. Nor does Guess *et al.* teach, suggest, or provide motivation for the rapid bioavailability, *i.e.* a greater C_{max} and/or substantially shorter T_{max}, of a drug of this formulation. Thus, the Guess *et al.* reference does not overcome the deficiencies of the principle reference. Accordingly, Applicants respectfully submit that claim 1 is patentable over Guess.

Bagchi *et al.* discuss a process for reportedly enhancing bioavailability of pharmaceutical agents with average particle diameters of less than 10 nm by chemically attaching the particles to photographic coupler molecules and surface modifiers which maintain average particle size of less than 100 nm. See Bagchi *et al.*, column 13, line 12 to column 14, line 4. Bagchi *et al.*, however, fail to teach, suggest, or provide motivation for a composition of selective cyclooxygenase-2 inhibitory compositions. Nor does Bagchi *et al.* teach, suggest, or provide motivation for the rapid bioavailability, *i.e.* a greater C_{max} and/or substantially shorter T_{max}, of a drug having an average particle size of greater than 100 nm. Accordingly, Applicants respectfully submit that amended claim 1 requiring a is patentable over Bagchi *et al.*

Further, one skilled in the art would not be led to practice the invention of claim 1 even if Black's disclosure is considered in view of Guess *et al.* and Bagchi *et al.* Nothing in the combined references remotely teaches or suggests a composition with rapid bioavailability, and comprising selective cyclooxygenase-2 inhibitory low water soluble drug with D₉₀ particle size of about 450 nm to about 900 nm. Although the references may arguably show a general teaching with regard to the bioavailability of drugs with an average particle size less than 100 nm, the references, either alone or in combination, fail to teach all of the claim limitations of the present invention. Accordingly, Applicants respectfully submit that amended claim 1 is patentable over Black in view of Guess *et al.* and Bagchi *et al.* Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is requested.

B. Claims 2-6, 8-11, 15-19 and 27

Claims 2-6, 8-11, 15-19 and 27 depend directly or indirectly from claim 1, and therefore are patentable over Black in view of Guess *et al.* and Bagchi *et al.* for at least the same reasons as claim 1.

C. Claim 20

Claim 20 is directed to a method of analgesia comprising oral administration of a selective cyclooxygenase-2 inhibitory low water soluble drug with D₉₀ particle size of about 450 nm to about 900 nm and a vasomodulator or alkylxanthine compound. The language of claim 20 tracks the language of claim 1. Thus, claim 20 is patentable over Black in view of Guess *et al.* and Bagchi *et al.* for at least the same reasons as claim 1.

D. Claims 21-26 and 28

Claims 21-26 and 28 depend directly or indirectly from claim 20, and therefore are patentable over Black in view of Guess *et al.* and Bagchi *et al.* for at least the same reasons as claim 20.

E. Claim 29

Claim 29 is directed to a composition comprising a selective cyclooxygenase-2 inhibitory low water soluble drug with D₉₀ particle size of about 450 nm to about 900 nm and a vasomodulator or alkylxanthine compound. The language of claim 29 tracks the language of claim 1. Thus, claim 29 is patentable over Black in view of Guess *et al.* and Bagchi *et al.* for at least the same reasons as claim 1.

F. Claims 30-32, 34-37 and 41-45

Claims 30-32, 34-37 and 41-45 depend directly or indirectly from claim 29, and therefore are patentable over Black in view of Guess *et al.* and Bagchi *et al.* for at least the same reasons as claim 29.

G. Claim 46

Claim 46 is directed to a method of analgesia comprising oral administration of a selective cyclooxygenase-2 inhibitory low water soluble drug with D₉₀ particle size of about 450 nm to about 900 nm and a vasomodulator or alkylxanthine compound. The language of claim 46 tracks the language of claim 1. Thus, claim 46 is patentable over Black in view of Guess *et al.* and Bagchi *et al.* for at least the same reasons as claim 1.

H. Claims 47-54

Claims 47-54 depend directly or indirectly from claim 46, and therefore are patentable over Black in view of Guess *et al.* and Bagchi *et al.* for at least the same reasons as claim 46.

I. Claim 55

Claim 55 is directed to a composition comprising a selective cyclooxygenase-2 inhibitory low water soluble drug with D₉₀ particle size of about 450 nm to about 900 nm and a vasomodulator or alkylxanthine compound. The language of claim 55 tracks the language of claim 1. Thus, claim 55 is patentable over Black in view of Guess *et al.* and Bagchi *et al.* for at least the same reasons as claim 1.

J. Claim 57

Claim 57 is directed to a method of analgesia comprising oral administration of a selective cyclooxygenase-2 inhibitory low water soluble drug with D₉₀ particle size of about 450 nm to about 900 nm and a vasomodulator or alkylxanthine compound. The language of claim 57 tracks the language of claim 1. Thus, claim 57 is patentable over Black in view of Guess *et al.* and Bagchi *et al.* for at least the same reasons as claim 1.

III. Rejection of claims 1-58 under 35 U.S.C. § 101

Claims 1-58 have been provisionally rejected under the statutorily-created double patenting doctrine in view of U.S. Patent Application No. 09/874,504. Because no subject matter of either application has yet been found to be allowable, Applicants submit that this rejection is premature. Applicants will address the rejection to the extent necessary once the claims have been found to be otherwise allowable.

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In view of the foregoing amendments and remarks, Applicants submit that the claims are in condition for allowance.

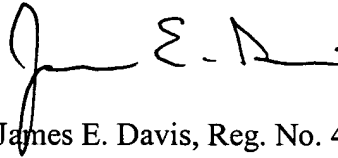
Applicants hereby request a 3-month extension to reply to the June 17, 2004 Office action, and have enclosed a check to cover that fee. Applicants do not believe that they owe any other fee in connection with this filing. If, however, Applicants do owe any such fee(s), the

Amendment B
Appl. No. 09/874,504
December 17, 2004

Commissioner is hereby authorized to charge that fee(s) to Deposit Account No. **08-0750**. In addition, if there is ever a deficiency or overpayment of fees in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **08-0750**.

The Examiner is requested to call the undersigned if any questions arise that can be addressed over the phone to expedite examination of this application.

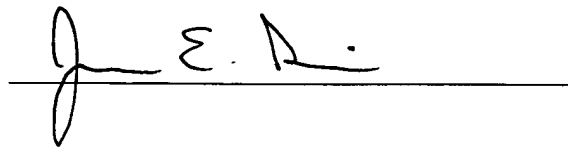
Respectfully submitted,



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I certify that this correspondence is being deposited with the U.S. Postal Service on **December 17, 2004** with sufficient postage as first class mail (including Express Mail per MPEP §512), and addressed to **Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450**.



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